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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/550,857	04/17/2000	Thomas Buch-Rasmussen	NN 26	1708

26137 7590 09/10/2004

PATENT DEPARTMENT
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EXAMINER	
WARD, PAUL V	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/550,857	BUCH-RASMUSSEN ET AL.	
	Examiner	Art Unit	
	PAUL V WARD	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2003*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-14,16-35 and 59-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-14,16-35 and 59-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claim 6, which was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim 3, has been overcome by applicant's amendment in canceling claim 6.

Claim Rejections - 35 USC § 112

Applicant's amendment has overcome the rejection of Claim 11 in which the claim was dependent on a cancelled claim and for reciting the limitation "pellet" for which there was insufficient antecedent basis.

Response to Amendment filed November 25, 2003

In regards to the rejection of claims 1-7, 9-14, 16-35, 39-55 and 59 under 35 U.S.C. 103(a) as being unpatentable over Roser in view of Bar-Shalom, Applicant's amendment filed November 25, 2003 has been fully considered but not persuasive. The rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated July 1, 2003.

Response to Arguments filed November 25, 2003

Applicant's arguments filed November 25, 2003 have been fully considered but they are not persuasive.

In response to Applicant's argument that Roser does not teach or suggest HDC compositions with the therapeutic agent with an amount above 20% could be used in a

needle-shaped pharmaceutical composition. On page 24, lines 29-31, Roser teaches that more than 20% weight percentage of organic molecules can be incorporated into the HDC delivery system. Further, Roser teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e., by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery systems can be tailored to have precise properties . . . ." . (See page 22, line 29 to page 23, line 3). Thus, it would be obvious to one of skill in the art at the time the invention was filed to distribute therapeutic agents above 20% homogenously throughout the compositions as such compositions are suitable materials that are hard to formulate for controlled, pulsatile or delayed release. Therefore, Roser provides proper motivation to make and use the recited invention.

In response to Applicant's argument that Roser nor Roser in view of Bar-Shalom teach or suggest compositions with the requisite intrinsic strength to be useful as needles. On page 22, line 29 to page 23, line 3, Roser teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e., by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery system can be tailored to have precise properties . . . ." . It would be obvious to one of skill in the art at the time the invention was filed to modify the particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form, including a needle, for use in controlled pulsative or delayed release of guest substances. Thus, Rose and Roser in view of Bar-Shalom, provide proper motivation to make and use the recited invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-14, 16-35, 39-55, 59 and 60-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser (previously cited).

Applicants claim solid pharmaceutical compositions having the shape of a needle for parenteral injection with (a) a binder that is at least 0.5% by weight of the composition comprising at least one non-crystallization agent and at least one carbohydrate-binding agent, and (b) at least one therapeutic agent that is at least 40% by weight of the composition, such that the therapeutic agent is distributed homogenously throughout the composition. In addition, Applicant claims compositions with specific physical properties, such as binders that can withstand a pressure force of at least 5 or 10 Newtons, binders that remain in an amorphous matrix for at least 6 months at ambient temperature, binders with a glass transition temperature of at least 30°C and compositions with specific viscosities at a certain temperature range. Applicant also claims methods to make such compositions by mixing, shaping and cooling. Finally, Applicant claims methods for injecting such compositions using an ejection device.

Roser, as set forth in the Office Action mailed July 1, 2003, is incorporated herein as set forth supra. Roser teaches solid dose delivery system comprising an active

agent and a glassy vehicle that may be a carbohydrate. Further, Roser teaches inclusion of sugar alcohols, which are non-crystallization agents of the claims. The composition may be formulated in various shapes, including as a needle. Any of a number of therapeutic agents may be employed. (See the claims). The Roser method of preparation includes mixing, shaping and drying (Claim 43). Roser teaches administration to animals, as well as human patients. (See pages 6-7). On page 7, lines 9-29, Roser teaches that it would be advantages to provide solid drug delivery systems of defined size, shape, density and dissolution rate, to ensure a more uniform distribution. In addition, Roser teaches that small delivery system size would also increase the comfort of the administration and minimize tissue damage. Further, Roser teaches on page 24, lines 29-31 that more that 20% weight percentage of organic molecules can be incorporated into the HDC delivery systems. Still further, Rose teaches that the HDC delivery system are particularly suited for use in controlled, pulsative or delayed release of guest substances, which may be incorporated in the HDC delivery system. (See page 20, line 21 to page 27). Roser also teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e., by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery systems can be tailored to have precise properties . . .". (See page 22, line 29). On page 25, lines 15-18, Roser teaches that the guest substance, i.e., therapeutic agent, can be incorporated into either the pre-melted HDC formulation, or stirred into the cooling HDC met before quenching. Moreover, Roser teaches that the guest substance can be easily incorporated either

from solution or as a particle suspension. (See page 26, lines 6-8). "The HDC melts are excellent solvents for many organic molecules. This makes them particularly suitable for use in delivery of bioactive materials otherwise difficult to formulate". (See page 24, lines 26-29).

Roser does not specifically state that the therapeutic agent should be at least 40% of the composition. In addition, Rose may not explicitly disclose each of the ingredients or formulation details as claimed.

It would have been obvious for a person of ordinary skill in the art at the time of the invention to increase the concentrations of the therapeutic agent. Roser teaches that more than 20% of the organic molecules can be incorporated into the delivery system. Therefore, one of ordinary skill in the art would have been motivated and would have a reasonable expectation of success in making and using a composition with at least 40% weight percentage of organic molecules in the compositions to (1) maximize the amount of therapeutic to be delivered and to minimize the size of the composition, (2) increase the comfort of administration and reduce tissue damage, (3) optimize the effectiveness of the composition, (4) modify a particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form, (5) minimize the amount of pain and tissue damage, and (6) distribute the therapeutic agent homogenously throughout the composition. Moreover, in the absence of unexpected results or proof to the contrary, the prior art renders obvious Applicant's invention. Therefore, one of ordinary skill in the art would have been

motivated and had a reasonable expectation of success to make and use the specific compositions of the present invention.

Claims 1-7, 9-14, 16-35, 39-55, 59 and 60-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, in view of Bar-Shalom(N), both previously cited.

As set forth supra, Applicants claim solid pharmaceutical compositions having the shape of a needle for parenteral injection with (a) a binder that is at least 0.5% by weight of the composition comprising at least one non-crystallization agent and at least one carbohydrate-binding agent, and (b) at least one therapeutic agent that is at least 40% by weight of the composition, such that the therapeutic agent is distributed homogenously throughout the composition. In addition, Applicant claims methods to make and use such compositions.

Roser, as set forth supra, teaches solid dose delivery system comprising an active agent and a glassy vehicle that may be a carbohydrate. Further, Roser teaches inclusion of sugar alcohols, which are non-crystallization agents of the claims. The composition may be formulated in various shapes, including as a needle. Any of a number of therapeutic agents may be employed. (See the claims). The Roser method of preparation includes mixing, shaping and drying (Claim 43). Roser teaches administration to animals, as well as human patients. (See pages 6-7). On page 7, lines 9-29, Roser teaches that it would be advantages to provide solid drug delivery systems of defined size, shape, density and dissolution rate, to ensure a more uniform

distribution. In addition, Roser teaches that small delivery system size would also increase the comfort of the administration and minimize tissue damage. Further, Roser teaches on page 24, lines 29-31 that more that 20% weight percentage of organic molecules can be incorporated into the HDC delivery systems. Still further, Rose teaches that the HDC delivery system are particularly suited for use in controlled, pulsative or delayed release of guest substances, which may be incorporated in the HDC delivery system. (See page 20, line 21 to page 27). Roser also teaches that the properties of HDC are easily manipulated by slight alterations in composition, i.e., by varying the modifications of a particular carbohydrate or by combining a variety of different HDCs, thus the "HDC delivery systems can be tailored to have precise properties . . .". (See page 22, line 29). On page 25, lines 15-18, Roser teaches that the guest substance, i.e., therapeutic agent, can be incorporated into either the pre-melted HDC formulation, or stirred into the cooling HDC met before quenching. Moreover, Roser teaches that the guest substance can be easily incorporated either from solution or as a particle suspension. (See page 26, lines 6-8). "The HDC melts are excellent solvents for many organic molecules. This makes them particularly suitable for use in delivery of bioactive materials otherwise difficult to formulate". (See page 24, lines 26-29).

Roser does not specifically state that the therapeutic agent should be at least 40% of the composition, and that it need to be a therapeutic agent capable of penetrating the skin or mucosa. In addition, Rose may not explicitly disclose each of the ingredients or formulation details as claimed.

Bar-Shalom, on page 6, lines 26-34, teaches solid pharmaceutical compositions with a shape and consistency enabling it to penetrate the skin, consisting essentially of the active drug substance. Bar-Shalom teaches that such compositions must have the sufficient strength to enable penetration of the skin or mucosa. Thus, various materials can be added to the compositions, including carbohydrates, such as polysaccharides, glucose, agarose and cyclodextrin, in crystalline or caramelized form. (See page 16, line 23 to page 17, line 10).

It would have been obvious to one of skill in the art to make and use the compositions of the present invention to make and use the pharmaceutical compositions of the present invention wherein the therapeutic agent is at least 25% of the composition by weight. Roser teaches pharmaceutical compositions comprising all of the disclosed ingredients. Bar-Shalom teaches that such pharmaceutical compositions require only enough binder to give sufficient strength to penetrate the skin or mucosa. The ratios of binder to therapeutic agent as well as the formulation details are considered to have been obvious over the overall teaching of Roser in view of Bar-Shalom, for the purpose of optimizing the effectiveness of the composition and of minimizing the amount of pain and tissue damage. It would have been obvious to one of skill in the art at the time the invention was filed to modify the particular carbohydrate or combine a variety of different HDCs to achieve a delivery system that can be molded into any shape or form, inkling a needle, for use in controlled, pulsatile or delayed release of guest substances. Further, it would have been obvious to one of ordinary skill in the art to distribute therapeutic agents homogenously throughout the

compositions as such compositions are suitable materials that are hard to formulate for controlled, pulsatile or delayed release. Moreover, in the absence of unexpected results or proof to the contrary, the prior art renders obvious Applicant's invention.

Conclusion

Claims 1-7, 9-14, 16-35, 39-55, 59 and 60-68 are pending. Claims 1-7, 9-14, 16-35, 39-55, 59 and 60-68 are rejected. No claims are allowed.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL V WARD whose telephone number is 571-272-2909. The examiner can normally be reached on M-F 8 am to 4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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